Systemic Protein Factors as Modulators of the Aging Neurogenic Niche

Grant Award Details

Systemic Protein Factors as Modulators of the Aging Neurogenic Niche

Grant Type: Basic Biology II

Grant Number: RB2-01637

Project Objective: The PI is identifying soluble protein factors in blood that can either promote or inhibit stem cell activity in the brain. Specifically, the PI is looking at dementia and age-related cognitive decline.

Investigator:

Name:	Tony Wyss-Coray
Institution:	Palo Alto Veterans Institute for Research
Type:	PI

Disease Focus: Alzheimer's Disease, Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $1,159,806

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: Systemic Protein Factors as Modulators of the Aging Neurogenic Niche

Public Abstract: Approaches to repair the injured brain or even prevent age-related neurodegeneration are in their infancy but there is growing interest in the role of neural stem cells in these conditions. Indeed, there is hope that some day stem cells can be used for the treatment of spinal cord injury, stroke, or Parkinson's disease and stem cells are even mentioned in the public with respect to Alzheimer's disease. To utilize stem cells for these conditions and, equally important to avoid potential adverse events in premature clinical trials, we need to understand the environment that supports and controls neural stem cell survival, proliferation, and functional integration into the brain. This "neurogenic" environment is controlled by local cues in the neurogenic niche, by cell-intrinsic factors, and by soluble factors which can act as mitogens or inhibitory factors potentially over longer distances. While some of these factors are starting to be identified very little is known why neurogenesis decreases so dramatically with age and what factors might mediate these changes. Because exercise or diet can increase stem cell activity even in old animals and lead to the formation of new neurons there is hope that neurogenesis in the aged brain could be restored to that seen in younger brains and that stem cell transplants could survive in an old brain given the right "young" environmental factors. Indeed, our preliminary data demonstrate that systemic factors circulating in the blood are potent regulators of neurogenesis. By studying how the most promising of these factors influence key aspects of the neurogenic niche in vitro and in vivo we hope to gain an understanding about the molecular interactions that support stem cell activity and the generation of new neurons in the brain. The experiments supported under this grant will help us to identify and understand the minimal signals required to regulate adult neurogenesis. These findings could be highly significant for human health and biomedical applications if they ultimately allow us to stimulate neurogenesis in a controlled way to repair, augment, or replace neural networks that are damaged or lost due to injury and degeneration.

Statement of Benefit to California: In California there are hundreds of thousands of elderly individuals with age-related debilitating brain injuries, ranging from stroke to Alzheimer's and Parkinson's disease. Approaches to repair the injured brain or even prevent age-related neurodegeneration are in their infancy but there is growing interest in the role of neural stem cells in these conditions. However, to potentially utilize such stem cells we need to understand the basic mechanisms that control their activity in the aging brain. The proposed research will start to address this problem using a novel and innovative approach and characterize protein factors in blood that regulate stem cell activity in the old brain. Such factors could be used in the future to support stem cell transplants into the brain or to increase the activity of the brain's own stem cells.